

C1 d) contacting said immobilized polypeptide or said binding partner polypeptide with said sample; and

e) assaying the modification of at least one of the polypeptides by measuring the association of the [second] binding partner polypeptide to the first polypeptide.

C2 4. (Amended) The method of claim 3, wherein said label[s] on [the] said immobilized polypeptide is different from said label on said binding partner polypeptide [and binding partner second polypeptides are different].

C3 6. (Amended) The method of claim 3 or 4, wherein [said] a detectable signal is generated by an interaction between the label[s] on said immobilized polypeptide and the label on said binding partner polypeptide.

C4 8. (Amended) The method of claim 1, wherein said ~~association is measured by~~ monitoring the molecular mass of the [hybrid] species comprising the [second] binding partner polypeptide associated with the first polypeptide.

12. (Amended) The method of claim 1, wherein said step (e) comprises measuring the association [association is measured] using an antibody that binds to said first polypeptide or said binding partner polypeptide.

C5 13. (Amended) The method of claim 1, comprising the additional step, prior to step [(d)] (e), of contacting one or both of said ~~first and~~ [second] binding partner polypeptide(s) with an agent capable of covalently modifying one or both of said polypeptides.

Sub E3 14. (Amended) The method of claim 1, wherein ~~the immobilised polypeptide is the polypeptide~~ which is susceptible to covalent modification.

C6 16. (Amended) The method of claim 1, wherein said [assaying said modification] step [(d)] (e) comprises assaying [one of] a modification selected from the group consisting of: proteolysis, phosphorylation, acylation, glycosylation, farnesylation, geranylation, ubiquitination, prenylation, sentrinisation, [and] ADR-ribosylation [, or] and the reversal of any of these modifications.

C7 18. (Amended) A method for detecting or monitoring the activity of a modulator of a polypeptide modifying agent, comprising the steps of:

C17
providing a first polypeptide, and a second polypeptide, wherein
at least one of the polypeptides is susceptible to modification, and
the first and second polypeptides are capable of binding to each other, and covalent
modification of one or both of the polypeptides by the modifying agent results in modulation of
the binding of the polypeptides to each other;

allowing the polypeptides to bind to each other,
contacting the polypeptides with a modifying agent,
detecting modulation of the binding of the polypeptides to determine a reference signal
modulation,

contacting the polypeptides with a modifying agent and a candidate modulator of the
modifying agent, and

detecting modulation of binding of the polypeptides in the presence of said candidate
modulator, and comparing the modulation detected in the presence of said candidate modulator
with the reference signal modulation.

Please add new claim 20 as follows:

C18
20. (New) The method of claim 1 wherein said covalent modification is an enzymatic
modification.

REMARKS

Claims 1-18 are pending. Claims 1-4, 6, 8, 12-14, 16 and 18 are amended and new claim
20 is added herein.

Support for the language of new claim 20 is found throughout the specification, but
specifically at page 4, lines 10 and 11, page 7, lines 22-24, and in the Examples.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-4, 6, 8, 12-14, 16 and 18 are rejected under 35 U.S.C. §112, second paragraph
for alleged lack of clarity.